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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,754	08/28/2001	Michele A. McTigue	0125-0016D3	3837

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,754	MCTIGUE ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-24* is/are rejected.

7)☒ Claim(s) *25 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action responds the Amendment received on January 22, 2004.

Preliminary Remark

Applicants' petition to revive the instant application from abandonment, via demonstration of mail-receipt, had been granted on February 6, 2004.

Specification

The specification is objected to because while the application complies with the Sequence Rules, page 10 of the specification, on 5th paragraph, recites primer sequences without their SEQ ID Number identifier. Applicants are advised to amend the specification to recite the proper SEQ ID Number identifier.

Claim Objections

The objection of claims 17, 22, and 23 for reciting the acronyms, "RTK," "PDGFR," and "VEGFR," without first reciting their full name, made in the Office Action mailed on July 1, 2003, is withdrawn in view of the Amendment received on January 22, 2004.

Claim Rejections - 35 USC § 112

The rejection of claims 17-26 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on July 1, 2003 is withdrawn in view of the Amendment received on January 22, 2004.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 17, 25, and 26 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9, 10, and 11 (respectively) of copending Application No. 09/939,833 (hereto referred to as '833 application), made in the Office Action mailed on July 1, 2003 is withdrawn because claims 9, 10, and 11 of the '833 application has been canceled during prosecution of the application.

Rejections – New Grounds

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Upon careful reconsideration of the application, the following rejection is applied.

Claims 17-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening compounds for receptor tyrosine kinase agonists (RTK) or RTK antagonists via use of a modified RTK polypeptide, wherein said RTK and

modified RTK polypeptide are VEGFR-2 polypeptide and modified VEGFR-2 polypeptide, does not reasonably provide enablement for a method for screening compounds for the genus of RTK agonists, using a modified RTK polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Instant claims are drawn to a method of screening for angonists or antagonists which interact with the kinase domain of a modified RTK polypeptide, wherein the modified RTK polypeptide embraces a genus of RTK polypeptides (instant claims 17-22) and particularly selected from the group consisting of VEGFR-1, VEGFR-2, PDGFR-α, PDGFR-β, stem cell growth factor receptor (c-kit), colony stimulating factor-1 receptor (CSF-1R/c-fms), IRK, FGFR-1, and VEGFR-2 (instant claims 23 and 24).

The claims embrace the use of a genus of modified RTK polypeptide for identifying compounds that act as its agonists or antagonist, but the specification as filed only discloses a single species of modified polypeptide, that is, VEGFR-2, thereby failing to enable a skilled artisan to practice the claimed method for identifying agonists or antagonists for any RTK polypeptides, commensurate in scope embraced by the instant claims for the following reasons.

Factors to be considered in determining whether a disclosure would require undue experimentation are summarized in In Re Wands (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). They include (A) the quantity of experimentation necessary, (B) the amount of direction or guidance presented, (C) the presence or absence of working examples, (D) the nature of the invention, (E) the state of the prior art, (F) the relative skill of those in the art, (G) the predictability or unpredictability of the art, and (H) the breadth of the claims.

The Wands factors are addressed as applicable.

(C) The Absence of working examples:

Modified IRK, FGFR-1, and VEGFR-2

Applicants' claims, particularly, claims 23 and 24 recite that there exists ***at least*** 8 species (if not more) within the claimed genus of RTK polypeptides. Instant claims therefore require: a) crystallization of a modified RTK polypeptide, said modified RTK polypeptide comprising a truncated KID that links domain α helix D and α helix E; and b) obtaining the crystallography coordinates for said modified RTK polypeptide.

However, the claims fail to fully enable the genus encompassed by the instant claims for the following reasons.

The specification only discloses a single species of the claimed modified RTK polypeptide, that is,VEGFR-2, wherein the modification comprises 50 residue-deletions from a kinase insert domain, identified by SEQ ID NO: 5. The specification does not give any example or disclosure regarding other species of modified RTK polypeptides embraced by the genus claims of 17-22 nor the species recited in the Markush Group of claims 23 and 24, *i.e* VEGFR-1, PDGFR-α, PDGFR-β, stem cell growth factor receptor (c-kit), colony stimulating factor-1 receptor (CSF-1R/c-fms), IRK, FGFR-1, and VEGFR-2. Further, the specification does not give any disclosure or examples of whether, if the above modified polypeptides were to be produced, such modified polypeptides would "crystallize" as the claims require that crystallography coordinates be obtained. It is important to note that the specification only contains x-ray

crystallography coordinates of the modified VEGFR-2 polypeptide. No other coordinates are given.

While the instant claims are rejected as failing to enable the scope of the claims embracing a genus, the rejection is based absence of Applicants' possession of the required elements (*i.e.,* genus of the modified RTK polypeptide) required by the claims. In regard to demonstrating that Applicants' were in possession of the elements, MPEP 2163(I) states that an applicants may show possession of the claimed invention in a variety of ways including description of actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

The specification only discloses the x-ray crystallography coordinates (derived from a crystallized structure) of the modified VEGFR-2 polypeptide comprising the deletion of 50 residues in the KID represented in SEQ ID NO: 5 (also identified as VEGFR-2Δ50 (Figure 7)). All of the examples and description point to a single species of VEGFR-2Δ50, such as isolation of the gene construct encoding the modified polypeptide (pages 11-12), the isolation and purification of the modified polypeptide (page 13), the kinetic assays (page 14, top), ***crystallization*** of the modified polypeptide (pages 16-20), structural determination (page 18). The specification lacks the evidence of reduction to practice for modified polypeptide of the species of VEGFR-1, PDGFR-α, PDGFR-β, stem cell growth factor receptor (c-kit), colony stimulating factor-1 receptor (CSF-1R/c-fms), IRK, FGFR-1, nor does the specification disclose

the structure of these species comprising the claimed truncation as well as their crystallized coordinates.

(D) Amount of Direction of Guidance:

The specification does not have any guidance in crystallization of species of other RTK polypeptides except for VEGFR-2 polypeptide.

(E) State of Prior Art:

Ohta et al. (US 2004/0059091 A1, published March 25, 2004), evidences the current status of protein crystallization, wherein the artisan state that the crystallization of a protein is, "***extremely difficult***," [0082].

(F) Skill level:

The skill level of the artisan in considered to be high.

(G) Unpredictability of the Art:

As already expressed by Ohta et al., the art of protein crystallization is extremely difficult, having an unpredictable outcome.

(H) Breadth of the Claims:

The breadth of the claims embraces a method of identifying compounds that act as agonists or antagonists to a genus of RTK polypeptide.

(A) Amount of Experimentation Necessary:

Because the specification nor the prior art have any working examples of crystallized modified RTK polypeptides, or their crystallography coordinates, the skilled practitioner would be required to produce the modified polypeptide of the claims first. However, based on the

extreme difficulties associated in producing crystallizing a protein, as expressed by Ohta et al., the skilled practitioner would not be able to practice the method commensurate in scope embraced by the claims without undue experimentation.

Conclusion

Claims 17-24 are rejected. Claims 25 and 26 are objected to for being dependent on a rejected base claim.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner can normally be reached from 8:30 a.m. to 6:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (517) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0507.

Young J. Kim
Patent Examiner
Art Unit 1637
4/19/04